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Twenty Lessons from Asbestos

A Bitter Harvest of Scientific Information

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It seems that we sometimes learn most from our worst mistakes. This certainly was the case in one of the greatest public health disasters in modern times — cigarette smoking. When the marked increase in cigarette use began after World War II, there were few predictions of what was to occur in the 1960s, 1970s and 1980s.

More recently, nature has been similarly unforgiving with regard to asbestos, perhaps because we were reluctant to heed the warnings that we were given. It was found in 1924, for example, that exposure to asbestos could result in fatal disease. In that year, the *British Medical Journal* published a report by W. E. Cooke of a young woman who had worked with asbestos and who had died with extensively scarred lungs. In 1927, again in the *British Medical Journal*, he gave the disease the name it still bears, Pulmonary Asbestosis. By 1930, additional British studies demonstrated that such scarring was very common among workers exposed to asbestos and these observations were soon confirmed in our country by Fulton, Dreessen, Lanza and their colleagues as well as by other scientists. By the mid-1930s it was well established that asbestos inhalation could frequently cause disease and that such disease might be fatal. Scientific research since then has added much information but, in a sense, this largely defined the different ways that asbestos could kill. Thus, in 1935, Lynch and Smith in the United States and Gloyne in Great Britain, noted the association of lung cancer and asbestos work, and during the 1940s and 1950s cases of pleural and peritoneal mesothelioma were seen in asbestos-exposed workers. This association was clarified and firmly established in the first half of the 1960s by Wagner, Selikoff, Churg, Newhouse and others. Additional neoplasms (malignant growths) — again, further ways of dying — were subsequently found related.

We are now in the midst of widespread asbestos disease resulting from exposures during the past 60 years. So far, W. J. Nicholson has calculated that there have been more than 100,000 deaths of asbestos-associated disease and that we may look forward to more than 350,000 additional such deaths before the effects of past exposures run their course. These projections are concerned with cancer deaths from occupational sources. There will be additional excess cancer deaths from non-occupational exposures, as well as deaths from asbestosis, but it has not yet been possible to make appropriate quantitative predictions. Further, the predictions are predicated on the assumption that, after 1980, asbestos exposure will have ceased. Initial experiences suggest that this was a dubious assumption, and that the tragic toll of death and disease will extend longer than we thought. Moreover, the 9,000 or so excess cancer deaths from occupational sources now seen each year are accompanied by many times that number of workers with asbestosis of greater or lesser severity, with greater or lesser disability, but insufficient to directly cause death.

Inevitably, the observation of so much serious disease has led to increased understanding of the circumstances in which it has occurred, (as scientists sought to evaluate those factors) both for prevention of disease in the future and to provide help to those for whom prevention is now too late. There has also been the hope that what we have learned from the asbestos tragedy will provide principles that may help to prevent similar disasters in the future.

TWENTY LESSONS

We have been taught much by the asbestos experience. This could be analyzed differently by the industrial hygienist, the regulator, corporate risk manager, clinician, industry executive, union official, pathologist, insurance company executive, lawyer, physiologist, economist, molecular biologist, and others. But perhaps the most pertinent lessons of all have been those gleaned from a public health point of view, from the perspective of how to prevent preventable disease. Twenty have been selected as being central to EPA responsibilities and concerns.

1. Latency: Although tissues and cells begin to react to the presence of inhaled asbestos fibers on a microscopic level within hours and days, clinical effects are not seen for years or decades. Even with the extensive exposure that was frequently found in asbestos factories in the past, it was commonplace to find no X-ray or pulmonary function change until five, ten, or more years had passed. These clinical probes are insensitive for demonstrating early changes. In one study of 1,117 asbestos insulation workers, regularly employed in the construction industry under circumstances in which significant exposure was the rule, more than half of those with less than 20 years from onset

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of exposure still had normal X-rays. After that point, most X-rays were abnormal. We should not expect to see early evidence of asbestotic change.

The same constraint is the rule for asbestos-associated cancer and for fatal asbestosis, as well. In a prospective study of 17,800 asbestos insulation workers, 1967-1976, relatively few asbestos- associated deaths were seen in less than 20 years from onset of their work exposure. Indeed, most deaths occurred 30, 40 or more years after exposure had occurred.

The disease and deaths now being experienced are the results of exposures in the 1940s and 1950s, with the 1960s beginning to make their contribution, the legacy of our mistakes of the past. Current exposures will not show their effects until the year 2010 and sequently.

2. Irreversible errors: Once exposure has occurred (with one exception so far, see below) the die seems cast. We know of no way to remove or neutralize fibers in the lung or in other tissues (to which some migrate). Whether this is because of the residual fiber tissue burden or because of cellular and molecular changes is not known. From the point of view of prevention of future disease, control of human exposure, wherever and whenever it is occurring, is an emergency. Sometimes this is not appreciated. Somehow when the disease effect is 30 years off, there is little sense of urgency. This is wrong. There might be less complacency about friable asbestos in schools and public buildings if this were better appreciated.

Dose-disease response: Less asbestos, less disease; more asbestos, more disease. This central fact provides guidance for what is to be done. We may not be able to control every last fiber in the environment, but we can take some comfort in knowing that as our engineering and regulatory measures become more and more effective, there will be less and less disease. However, the "dose" of asbestos is cumulative, with newly inhaled fibers added to the burden already present. Therefore, each opportunity for asbestos exposure should be controlled not only because of its own hazard, but because it would be adding to the risk from other sources. This is a good example of the correctness of the definition of dose as "intensity x time."

With many agents, it is very difficult to ascertain "dose" associated with disease being seen, since the exposures responsible for such disease occurred decades before, when measurements were not made. Seidman and his colleagues have recently reviewed a unique set of circumstances demonstrating the dose-disease response nature of asbestos disease. They traced the long-term mortality experience of a large group of asbestos factory workers employed during World War II. They were all exposed to the same fiber, making the same products, using the same machinery, in the same plant. They differed, however, in one respect. Because of wartime conditions, some worked for a day, a week, a month, several months. Others worked from the time the plant opened in 1941 to when it closed in 1954. Since the intensity, for the groups involved, was the same, dose was proportional to duration of exposure. Lung cancer incidence for the various groups increased with increasing dose.

4. Disease with brief exposure: There have been numerous reports of relatively brief exposure and the subsequent occurrence of disease. However, many reflected individual experiences and for diseases such as lung cancer, they did not "prove" an association with short exposure.

The risk of brief exposure became better established with the study of mesothelioma, a neoplasm which has few known causes in humans other than asbestos. When mesothelioma is found, prior asbestos exposure is looked for and usually found. When asbestos exposure occurs, there is significant risk of subsequent mesothelioma. The extraordinary relationship between asbestos exposure and mesothelioma was perhaps best considered by Cochrane and Webster. They interviewed 107 patients in whom the diagnosis of mesothelioma had recently been established by biopsy. In 106, potential prior exposure to asbestos was elicited. The experiences of Seidman et al (see above) have provided the necessary population-based data to confirm the keen clinical observations previously made.

The mechanism by which brief exposure subsequently results in disease is not known. It may be related to the retention of fibers in tissues but it may not. The same phenomenon is seen in bladder cancer following exposure to beta-naphthylamine or benzidine or in angiosarcoma of the liver after vinyl chloride exposure where there is no evidence for retention of the chemical carcinogens.

5. Disease with low-level exposure: The dose-response relationship for asbestos appears to be linear. This predicts disease with low exposures. The model has been shown to be correct. In 1965, Newhouse reported mesothelioma among individuals whose only known exposure had occurred as a result of residence in households of asbestos workers, or by virtue of living within a half-mile of an asbestos plant in London. Such family contact and neighborhood exposure mesothelioma has been widely confirmed and its importance documented. Of course, it can be argued that such exposure is not "low," particularly since it results in a significant amount of disease (in one current study, lung cancer risk appears to be about doubled and mesothelioma to be responsible for approximately 1% of deaths occurring 20 or more years following the initiation of household contact exposure).

What will happen at the lowest levels of exposure is still not known. There are other uncertainties. Brief exposure, if fairly intense, produces disease. Long-term exposure, at relatively low levels (household) produces disease. It is not known whether brief exposure to low levels will produce detectable disease. Complicating such analyses is the cumulative nature of even low-level exposure. The problem is not unique to asbestos; it is also the case with PCBs, dioxins, etc. This again points to the necessity for control of all sources.

6. Multiple factor interaction: It has long been suspected that much human disease from exogenous sources is multifactorial in nature. Asbestos taught us that this is indeed so. When the experiences of the 17,800 asbestos insulation workers, with smoking habits known and observed prospectively, were compared with those of 73,736 like men in the American Cancer Society's prospective study of cigarette smoking, a remarkable multiplicative effect was seen. Men who did not smoke and did not work with asbestos suffered 11 deaths per 100,000 man-years. For asbestos workers who did not smoke, it was five times as much, 58. On the other hand, individuals who smoked but did not work with asbestos had a death rate of 122 per 100,000 man-years, and men who had both exposures, asbestos and cigarette smoking, had 601. There is evidence that the same cigarette smoking-asbestos interaction may explain the increased risk of cancer of the esophagus, oropharynx and buccal cavity, and larynx. There is no such interaction, however, for mesothelioma, cancer of the stomach, colon-rectum or kidney — both smokers and non-smokers suffer equally.

Conclusions important for prevention may be drawn. First, all individuals known to have been exposed to asbestos should never start smoking or, if they are smoking, should stop immediately. This is particularly important since data indicate that there can be reversal of risk once smoking ceases. Asbestos insulation workers who stop smoking, after 5-10 years, have about one-third to

Two workers removing asbestos from a ceiling.

one-half the risk of lung cancer of their mates who continue to smoke. While cancer, once it occurs, is not reversible, cancer *risk* may be. A corollary conclusion, however is inherent in the above observations. Since smoking cessation will not affect risk of mesothelioma or the other neoplasms not associated with smoking, it will be equally necessary to control asbestos exposures. Both measures are needed.

7. Product use: For every worker employed in the manufacture of asbestos products, there may be 500 who would use them or be exposed indirectly during such use. It is therefore unfortunate that at the outset of our asbestos experience, we thought of "asbestos workers" — men and women employed in mining, milling or factory work. The first phase of asbestos exposure and accompanying disease was associated with *product manufacture*. Later, during the last 40 years or so, there was increasing attention to disease associated with *product use* in the construction industry, shipyards, powerhouses, chemical plants and refineries, brake maintenance and brake repair, etc. We are now entering a third phase — in which asbestos exposure will be associated with *environmental exposures*, during repair, renovation, removal, and maintenance of the asbestos put in place during Phase Two. We have learned the difficult lesson of not thinking of asbestos workers, but asbestos-exposed workers.

8. Industrial origin of environmental disease: The factory gate and the factory fence are porous. Almost all asbestos exposure is industrial in origin, although some fibers derive from erosion of natural outcroppings, and water may be contaminated as it filters through asbestos rock formations. Such environmental contamination is very limited, however, particularly in terms of disease.

9. Multiple effects/multiple agents: Asbestos can produce a variety of illnesses, ranging from pulmonary and pleural fibrosis to lung cancer, pleural and peritoneal mesothelioma, gastrointestinal cancer, cancer of the oropharynx and buccal cavity, laryngeal cancer, and kidney cancer. Other effects, too, are now being seen, including immunomodification and serological changes. The other side of the coin, important from a diagnostic point of view, is that virtually all of these diseases and modifications can be caused by other agents, as well. Even mesothelioma, so highly attributable to asbestos, can be found to have other causes. Already, erionite has been seen to produce pleural and peritoneal mesothelioma among residents of Cappadocia, Turkey, and there is considerable concern that other materials, particularly man-made fibers, may eventually be associated with mesothelioma risk.

10. Environmental persistence: It has been said that asbestos has "a half-life of infinity." This is remembered ruefully as one considers the 30,000,000 tons of asbestos put in place from 1900 to 1980, in our ships, buildings, schools, chemical plants, refineries, powerhouses, factories, etc. Approximately 700,000 tons of insulation materials were installed in the same period; much remains.

11. Complexity of initiation and promotion: There has been much scientific interest in recent years concerning the concept that carcinogenic agents may either initiate the cancer process or, once initiated by other agents, promote its development. Asbestos seems to do both, according to circumstances. Thus, for lung cancer, the data suggest that it acts as a promoter, multiplying the background risk at each attained age. A 50-year- old individual has a much greater background risk of lung cancer than, let us say, one who is 20. Asbestos, in each, multiplies that risk It therefore does not achieve very much to restrict hiring to older workers, in the hope that latency would give them a ver long life before lung cancer might strike. Two latencies have to be considered — background exposure and asbestos. This would apply, for example, to teachers in asbestos-laden schools. Their risk depends upon their age as well as their prior asbestos exposure. A 55-year-old teacher with only 10 years in such a school nevertheless has important risk.

On the other hand, since there is little background risk of mesothelioma, asbestos acts as an initiator with risk increasing with age by approximately a power of four. Again in school circumstances, this points to the importance of prevention of exposure of children, with long lives ahead of them.

12. Complexity of societal consequences It has long been a truism that, from an ecological and environmental point of view, everything is related to everything else. With asbestos, this dictum applies to other circumstances, as well. Current litigation has been marked by bankruptc of major industrial firms, thousands of lawyers face each other in courts clogge by suits seeking help and redress, insurance companies are concerned with potentially monumental costs. It has been variously estimated that asbestos disease payments to victims will range between 40 and 150 billion dollars. In addition, Professor William G. Johnson of Syracuse has calculated that social costs of asbestos disease due to previou exposure will total more than three hundred billion dollars. Industrial practices are changing, with the advent of substitute materials, many of untestec toxicity. Doubt has even been cast on the effectiveness and applicability of the workers compensation system.

We are also beginning to see another legal tangle, perhaps of equal or greater complexity, with legal battles shaping up over who is to pay for the expense associated with abatement of asbestos ir schools and public buildings.

13. Early utilization of industrial hygiene engineering: Failure to respond early to information concerning the disease potential of asbestos carried with it the omission of measures needed to control exposure. Asbestos became entwined in industrial procedures with hazards intact. When, decades later, there was increasing concern with disease

potential, it was doubly difficult to change uses and procedures integral with the entire fabric of industrial production. Moreover, since the industrial engineering measures that were needed were being telescoped into a relatively short period of time rather than having been accomplished over many years, attendant costs were correspondingly high. To further complicate matters, these costs had to be borne at a time when the product itself was being questioned and sales were decreasing.

14. Disadvantages of fragmentary regulatory approaches: There has been less than complete interaction and interdigitation of knowledge, experience, research, regulatory actions. Dreessen of the U.S. Public Health Service undertook a rather elegant study of asbestos disease potential in the early 30s (published in 1938). I expect that it was hardly known to the National Cancer Institute's Advisory Council when, in 1951, it rejected a proposal by Leroy U.Gardner, then dean of experimental dust disease pathologists, to study cancer potential of asbestos in animals (he had early hints of such findings in his pneumoconiosis experiments).

There has been less than complete integration of the interests and studies of the EPA, NIOSH, NIEHS, CPSC, NCI. Fortunately, mechanisms exist for such interdigitation.

15. Science is necessary but not sufficient: When, in the latter half of the 19th Century, it began to be found that serious human disease could be caused by exogenous agents (infectious) a revolution in scientific thinking began; there was now not only description, but causation. (It is instructive to appreciate how recent this has been; 1982 was only the one hundredth anniversary of the discovery of the tubercle bacillus by Koch.) It was soon found that the identification of causes could be followed by their control. Pasteurization of milk, sewer systems, and clean water supplies were put in place. In the first half of the 20th Century, we again applauded those who discovered still other causes of disease, often metabolic, endocrine, or nutritional.

The same approbation has not inevitably met those studies which have identified some of the newer exogenous causes of disease. The tobacco industry has given no testimonial dinners to the researchers who have shown that this year we might expect more than 100,000 deaths of lung cancer due to cigarette smoking (plus additional excess deaths of pancreas, bladder, oropharyngeal, esophageal and larynx cancers, plus deaths of cardiovascular disease and emphysema). As we consider 8-naphthalymine and benzidine, 4-aminobiphenyl, nickel smelting, arsenic, vinyl chloride, lead, cadmium, chromium, etc., we are reminded that, in the 1890s, there were no trade associations for the protection of the cholera vibrio or the tubercle bacillus, no firms producing salmonella, no public relations groups operating on behalf of the pneumococcus, the diphtheria or the staphylococcus.

It has become clear that, just as in the 1890s, scientific research is necessary for the identification of causes of disease. But the simple gathering of data is only one part of the process. Utilization of the information is also required. Regulatory measures are needed, often of considerable complexity.

16. Indoor air pollution: It took some little time before it became clear which agency was going to consider itself responsible for indoor air pollution with asbestos. The complexity of the problems being found make such bureaucratic reluctance understandable. Nevertheless, in view of the very large number of people involved, this has become increasingly important. Perhaps the late acceptance of responsibility, as well as the late identification by scientists of the potential importance, help to explain the paucity of exposure data now at hand.

17. Recruitment of constituencies: An important asbestos lesson, perhaps related to what has been said before about science being necessary but not sufficient, has been the increasing understanding that application of knowledge can be speeded when those who are directly affected have the information that intimately concerns them. OSHA operates best, perhaps, when both labor and industry are aware of the facts that form the background for OSHA regulations. EPA's requirements that parents and teachers be told of asbestos findings in schools, is of this genre. Control of asbestos exposure depends at least as much upon understanding at the shop floor, as upon intricate regulations ensconced in the *Federal Register*. If we don't have understanding of what has to be done on the part of supervisory personnel and workers, there will never be enough inspectors to insure safety. With understanding, we will need few.

All this translates into an important educational function for EPA!

HOW MANY ANGELS ON THE HEAD OF A THRESHOLD?

18. Disease: There are learned and often esoteric discussions of how much disease might be expected at very low levels of exposure. Calculations are made and projections offered. It will be very difficult to verify or contradict these. Epidemiologically, very large populations will be required, carefully defined as to biases and variables. Since few cases of disease are expected at such levels, it is unlikely that the vast resources necessary for these studies will ever be made available. Animal experiments at very low levels will always have the disadvantage of insecurity with regard to extrapolation to humans.

The discussions, while interesting and important from a regulatory point of view, nevertheless have an air of unreality at this moment, with workers still being exposed to permissible levels of more than 20 million fibers per day; these estimates refer to longer fibers and do not take into account the very much larger number of shorter ones which accompany them but are not counted. Concern about very low levels seems somewhat out of touch with reality while some schools have levels of 100 to 1,000 nanograms and while maintenance and repair work on asbestos materials is often undertaken without precautions or supervision.

19. Limitations of epidemiology: These are widely acknowledged — evidence is based upon human disease that has already occurred, available methods are insensitive in detecting other than very gross and marked effects, studies are not suitable for smaller populations, there is frequent lack of concomitant exposure data, etc. Further, with the inevitable biases and variability inherent in human population studies, residual uncertainties persist and sometimes the best that can be achieved is the acknowledgment of "associations" rather than definitive causation.

Yet for asbestos disease, epidemiology has served us well and we have had only limited assistance so far from animal studies. It is to be hoped that in coming years, with other agents, we will no longer have to depend so heavily on epidemiological studies of human experience.

20. The concept of "industry" identity: There is probably no such thing as a monolithic industry, each sector being identical with all others. Some industry units are knowledgeable, others not. Some are concerned and truly responsible, others couldn't care less. Who, then, speaks for "industry"? My own experience with asbestos problems indicates that trade associations do not always speak for the most knowledgeable and the most involved industry units. This can be an important disadvantage. □